Docket No. 335**5.1** Serial No.: 09/955,**357** 

T-792 P.003/018 F-407

## Amendments to the Specification

Please replace the title of the application, page 1, and page 2, line 1, with the following title:

"Methods and Computer Software Products for Association of Gene Expression with Genetic Variations"

Please replace the paragraph on page 9, line 24, with the following paragraph:

Microarray can be used in a variety of ways. A preferred microarray contains nucleic acids and is used to analyze nucleic acid samples. Typically, a nucleic acid sample is prepared from appropriate source and labeled with a signal moiety, such as a fluorescent label. The sample is hybridized with the array under appropriate conditions. The arrays are washed or otherwise processed to remove non-hybridized sample nucleic acids. The hybridization is then evaluated by detecting the distribution of the label on the chip. The distribution of label may be detected by scanning the arrays to determine fluorescence intensity distribution. Typically, the hybridization of each probe is reflected by several pixel intensities. The raw intensity data may be stored in a gray scale pixel intensity file. The GATCTM Consortium has specified several file formats for storing array intensity data. The final software specification is available at the GATCTM Consortium website www.gateconsortium.org and is incorporated herein by reference in its entirety. The pixel intensity files are usually large. For example, a GATC™ compatible image file may be approximately 50 Mb if there are about 5000 pixels on each of the horizontal and vertical axes and if a two byte integer is used for every pixel intensity. The pixels may be grouped into cells. (See GATCTM software specification). The probes in a cell are designed to have the same sequence; i.e., each cell is a probe area. A CEL file contains the statistics of a cell, e.g., the 75th percentile and standard deviation of intensities of pixels in a cell. The 50, 60, 70, 75 or 80th percentile of pixel intensity of a cell is often used as the intensity of the cell.

Please replace the paragraph on page 15, line 14, with the following paragraph:

FIG. 3 shows an exemplary computer network that is suitable for executing the computer software of the invention. A computer workstation 302 is connected with and controls a probe array scanner 301. Probe intensities are acquired from the scanner and may be displayed in a monitor 303. The intensities may be processed to make genotype calls (i.e., determining the genotype based upon probe intensities) on the workstation 302. The intensities may be processed and stored in the workstation or in a data server 306. The workstation may be connected with the data server through a local area network (LAN), such as an Ethernet 305. A printer 304 may be connected directly to the workstation or to the Ethernet 305. The LAN may be connected to a wide area network (WAN), such as the Internet 308, via a gateway server 307 which may also serve as a firewall between the WAN 308 and the LAN 305. In preferred embodiments, the workstation may communicate with outside data sources, such as the National Biotechnology Information Center, through the Internet. Various protocols, such as FTP and HTTP, may be used for data communication between the workstation and the outside data sources. Outside genetic data sources, such as the GenBank 310, are well known to those skilled in the art. An overview of GenBank and the National Center for Biotechnology information (NCBI) can be found in the web site of NCBI (http://www.nebi.nlm.nih.gov).

Please replace the paragraph on page 18, line 18, with the following paragraph:

The resulting derived nucleic acid sample may be pooled, purified, fragmented and labeled (504) and then hybridized with an array (507). The hybridization is detected and analyzed (508, 509, and 510). The arrays may be gene expression arrays such as the GeneChip(R) HuGeneFL array (Affymetrix, Inc.), genotyping arrays or arrays have having the eability capability of detecting sequence variations as well as quantifying the sequence variations. In some embodiments, the arrays are custom designed based upon

Docket No. 3355.1 Serial No.: 09/955,357

T-792 P.005/018 F-407

the information about the genes, genic genomic regions or other regions of interest (505) and (506). Methods for nucleic acid probe array design, genotyping detection, hybridization, signal detection, and various data analysis methods are described earlier and in, for example, references previously incorporated by reference.